



Gene Sequencing

February 18, 2004



On February 18, 2004, the U.S. Environmental Protection Agency and Department of Energy signed a Memorandum of Understanding to expand the research collaboration of both agencies to advance biological, environmental, and computational sciences for protecting human health and the environment and fostering a secure, reliable, and economically sustainable energy system. This fact sheet describes a collaborative research area and the expertise each agency brings.

Computational biology is a multi-disciplinary science that takes advantage of new technologies to understand the molecular mechanisms underlying the environmental transformation, organismal metabolism, toxicity, and adverse outcomes of chemicals. Using approaches derived from modern computational methods, medicinal chemistry, molecular biology and systems biology, computational biology allows us to address the questions of "when and how" to test specific chemicals for hazards and for improving quantitative risk assessments of chemicals and microbial human pathogens. Gene sequencing holds the potential to reveal molecular pieces of the toxicity pathway which is critical to these questions. This is particularly important for sub-mammalian species, for which such information lags considerably behind mammals.

How sequencing genes will protect the environment

The collaboration between EPA and DOE will produce DNA sequence data on organisms of special importance to EPA's effort to apply molecular data to the prediction of toxicity, characterization of exposure, and, ultimately, integration in ecological risk assessments. These organisms include the fathead minnow (*Pimephales promelas*), the African clawed frog (*Xenopus tropicalis*) and the freshwater crustacean *Daphnia pulex*.

The Department of Energy's Joint Genome Institute is expanding its mission to bring high-throughput DNA sequencing and bioinformatics expertise to the greater academic, government and industrial scientific community. DOE is beginning its partnerships with EPA by collaborating on gene sequencing projects.



The fathead minnow and aquatic toxicity

The fathead minnow (*Pimephales promelas*) has been used for decades as a sentinel for aquatic ecological risk assessment and remains a standard model for aquatic toxicity testing. The fish is used in a broad range of environmental analyses including

effluent monitoring, pesticide registration, and evaluation of endocrine-disrupting chemicals. Having the gene sequence for this species has both economic and regulatory benefits for EPA and DOE and other agencies and research organizations. A fuller set of *Pimephales* gene sequences will allow government and industry to develop more tools for predicting toxicity in aquatic organisms and improving aquatic ecosystems monitoring. Such new tools will provide reliable science to support sound regulatory determinations and environmental decisions.

EPA will collaborate with DOE on the development and sequencing of complementary DNA libraries from different tissues of control fathead minnows at different developmental stages as well as sequencing of libraries from tissues of minnows exposed to chemicals stressors of particular programmatic importance. This, in turn, will aid in constructing the first large scale cDNA microarrays for research use by environmental scientists.

Understanding embryonic development with *Xenopus laevis*

Xenopus laevis has long served as a model for the study of embryonic development and developmental toxicology. Biological processes in the frog provide a great deal of insight into human biological processes. EPA will join DOE and the international amphibian research community in work already in progress, with the whole genome sequencing of *Xenopus tropicalis*, an organism closely related to *Xenopus laevis*.



Small *Daphnia* may uncover large issues

DOE's plans to sequence the genome for *Daphnia pulex*, an invertebrate organism, will contribute unique data for EPA's ecological risk assessments and historical use of invertebrate toxicity tests. Mechanisms of toxicity in invertebrates may relate well to that of aquatic vertebrates (e.g., fathead minnow) and thus support species extrapolation hypotheses. The sequencing is part of plans developed under the International Daphnia Genomics Consortium, which includes DOE and EPA molecular biologists.